Attorney Docket No. GENE-120/02US

THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of DIGGANS et al.

Confirmation No.: 1710

Serial No.:

10/580,423

Group Art Unit:

1631

Filed:

May 24, 2006

Examiner:

To Be Assigned

For:

METHODS FOR MOLECULAR TOXICOLOGY MODELING

U.S. Patent and Trademark Office Customer Service Window Randolph Building 401 Dulany Street Alexandria, VA 22314

INFORMATION DISCLOSURE STATEMENT TRANSMITTAL

Enclosed is an Information Disclosure Statement and accompanying Form PTO/SB/08 for the above-identified patent application.

In accordance with 37 C.F.R. §1.97(b), no additional fee for [X]submission of the IDS is required.

The Director is hereby authorized to charge any appropriate fees under 37 C.F.R. §§1.16, 1.17, and 1.21 that may be required by this paper, and to credit any overpayment, to Deposit Account No. 50-1283.

Dated: 3-12-07

Respectfully submitted,

COOLEY GODWARD KRONISH LLP

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PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

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SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT UNDER 37 C.F.R. §1.97(b)

In accordance with the duty of disclosure set forth in 37 C.F.R. §1.56, Applicant(s) hereby submits the following information in conformance with 37 C.F.R. §\$1.97 and 1.98.

- [X] Pursuant to 37 C.F.R. §1.98, a copy of each non-US patent document cited in the attached Form PTO/SB/08 is enclosed.
- [X] No copies of any U.S. patents or U.S. patent application publications listed on the attached Form PTO/SB/08 are being provided pursuant to 37 C.F.R. §1.98.
- [X] The present application and its related applications generally disclose toxicology modeling of various tissues or cells, e.g., heart, kidney, liver, or primary hepatocytes using gene expression data. As such, some of the nucleic acid sequences disclosed in this application may overlap with those disclosed in other related applications. For the Examiner's convenience, a list of the co-pending applications is presented below.

APPLICATION SERIAL NO.	TITLE	APPLICATION DATE	TISSUE
09/917,800	Molecular Toxicology Modeling	July 31, 2001	Liver
10/501,933	Molecular Hepatoxicology Modeling	Jan. 31, 2003	Liver

APPLICATION SERIAL NO.	TITLE	APPLICATION DATE	TISSUE
11/059,535	Molecular Toxicology Modeling	Feb. 17, 2005	Liver
10/152,319	Molecular Toxicology Modeling	May 22, 2002	Kidney
10/515,325	Molecular Nephrotoxicology Modeling	Nov. 24, 2003	Kidney
11/036,196	Molecular Toxicology Modeling	Jan. 18, 2005	Kidney
11/642,647	Molecular Nephrotoxicology Modeling	Dec. 21, 2006	Kidney
10/338,044	Molecular Cardiotoxicology Modeling	Jan. 8, 2003	Heart
10/541,937	Molecular Cardiotoxicology Modeling	Jan. 8, 2004	Heart
11/600,759	Cardiotoxin Molecular Toxicology Modeling	Nov. 17, 2006	Heart
10/357,507	Primary Rat Hepatocyte Toxicology Modeling	Feb. 4, 2003	Hepatocyte
10/515,373	Primary Rat Hepatocyte Toxicity Modeling	Aug. 9, 2004	Hepatocyte
10/580,423	Methods For Molecular Toxicology Modeling	Nov. 24, 2004	General
11/547,759	Hepatotoxicity Molecular Models	Apr. 7, 2005	Liver

- [X] In particular, the following publications were cited by the U.S. Patent Examiner in U.S. application 09/917,800:
 - 1. U.S. 5,811,231
 - 2. U.S. 6,372,431
 - 3. U.S. 6,218,122
 - 4. Lashkari et al. PNAS, vol. 94: 13057-13062, 1997
- [X] The following publications were cited by the Examiner in U.S. application 10/152,319:
 - 1. "nephrotoxic" definition, Merriam-Webster online dictionary, 2005, on the world wide web at http://www.m-w.com/cgi-bin/dictionary?

 Book=Dictionary&va=nephrotoxic

- 2. Yamaki *et al.* Cellular mechanism of lithium-induced nephrogenic diabetes insipidus in rats. American Journey of Physiology Renal Physiology, 1991. Vol. 261, F505-F511
- [X] The following publication was cited by the Examiner in U.S. application 10/301,856:
 - 1. Konstandi *et al.* Stress-mediated modulation of B(alpha)P-induced hepatic CYP1A1: role of catechomaines, 2004 Chemico-Biological Interactions, vol. 147
- [X] The following publication was cited by the Examiner in U.S. application 10/191,803:

U.S. 6,461,807

- [X] The following publications were cited by the Examiner in U.S. application 10/357,507:
 - 1. U.S. 6,203,987
 - 2. Peng et al. JBC, 271(6):3324-3327
 - 3. GenBank Acc. No. AA799479 (4/30/1998)
 - 4. GenBank Acc. No. AI177366 (1/20/1999)
 - 5. GenBank Acc. No. M25823 (4/27/1993)
 - 6. GenBank Acc. No. AA891812 (1/25/1999)
- [X] References were also cited in related or corresponding foreign applications. The following publications were cited in a foreign search or examination report corresponding to PCT/US01/23872.
 - 1. Raburn *et al.*, "Stage-specific expression of B Cell Translocation Gene 1 in rat testis," Endocrinology 136(12):5769 5777, 1995
 - 2. GenBank Accession No. L26268, Raburn *et al.*, "Rattus norvegicus antiproliferative factor (BTG1) mRNA," January 26, 1996
 - 3. Bissig *et al.*, "Functional expression cloning of the canalicular sulfate transport system of rat hepatocytes," J Biol. Chem 269(4):3017-3021, 1994
 - 4. GenBank Accession No. L23413, Bissig *et al.*, "Rattus norvegicus sulfate anion transporter (sat-1) mRNA," April 12, 1994
 - 5. WO 00/12760

- 6. Farr *et al.*, "Concise review: gene expression applied to toxicology," Toxicol Sci 50(1):1-9, 1999
- 7. Nuwaisyr *et al.*, "Microarrays and toxicology: the advent of toxicogenomics," Molecular Carcinogenesis 24(3):153 159, 1999
- [X] References were also cited in related or corresponding foreign applications. The following publications were cited in a foreign search or examination report corresponding to PCT/US02/21735.
 - 1. US 2001/0039006 A1
 - 2. US 2002/0119462 A1
 - 3. Grigg *et al.* Environmental Health Institute to use gene chips to evaluate chemicals for potential harm to humans. NIEHS, 29 February 2000
 - 4. US 6,228,589
- [X] The following publications were cited in a foreign search or examination report corresponding to EP 01959321.9.
 - 1. Markovich *et al.*, "Heavy metals mercury, cadmium, and chromium inhibit the activity if the mammalian liver and kidney sulfate transporter sat-1," Toxicol. Appl. Pharmacol. 154:181-187 (1999)
 - 2. WO 99/58670
 - 3. WO 93/01205
 - 4. WO 99/43345
 - 5. Berbner *et al.*, "induction of cytochrome P450 IA and NDA damage in isolated rainbow trout (Onchorhynchus mykiss) hepatocytes by 2, 3, 7, 8-tetrachlorodibenzo p-dioxin," Biomarkers 4: 214-228 (1999)
 - 6. Bogdan, "Human carbon catabolite repressor protein (CCR4)-associative factor 1: cloning, expression and characterization of its interaction with the B-cell translocation protein BTG1," Biochem. J. 336:471-481 (1998)
- [X] The following publications were cited in a foreign search or examination report corresponding to PCT/US03/03194:
 - 1. U.S. 6,218,122
 - 2. U.S. 2001/0049139

- [X] The following publications were cited in a foreign search or examination report corresponding to Canadian application 2,447,357
 - 1. WO 01/32928, 05/11/01, Far et al.
 - 2. Fielden *et al.* Changes and limitations of gene expression profiling in mechanistic and predictive toxicology, Toxicol. Sci. 60: 6-10
 - 3. Affymetrix Rat Toxicology U34 Datasheet, released 08/99
- [X] The following publications were cited in a foreign search or examination report corresponding to EP 02771863.4
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 - 2. Database Geneseq [online], "Sindbis virus genomic cDNA PCR primer SEQ ID NO:3," Database Accession No. AAZ92894, retrieved from EBI Accession No. GSN:AAZ92894 (2000)
 - 3. Bulera, S.J., *et al.*, RNA expression in the early characterization of hepatotoxicants in wistar rats by high-density DNA microarrays. Hepatology, 33:1239-1258, (2001)
 - 4. Nuwaisyr *et al.*, "Microarrays and toxicology: the advent of toxicogenomics," Molecular Carcinogenesis 24(3):153-159, 1999.
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 - 6. Burchiel *et al.*, Analysis of genetic and epigentic mechanisms of toxicity potential roles of toxicogenomics and proteomics in toxicology. Toxicol. Sci., 59: 193-195 (2001)
 - 7. WO 97/13877
 - 8. WO 01/25473
 - 9. WO 99/27090
- [X] The following publications were cited in a foreign search or examination report corresponding to PCT/US02/16173:
 - 1. U.S. 6,228,589
 - 2. U.S. 6,365,352
 - 3. U.S. 6,403,778
 - 4. Kim *et al.*, Fumonisin B1 induces apoptosis in LLC-PK1 renal epithelial cells via a sphinganine and calmodulin dependent pathway. Toxicology and Applied Pharmacology 176:118-126 (2001)
 - 5. Yang et al., Differential regulation of COX-2 expression in the kidney by lipoplysacc: role of CD14. Am J Physiology 277(1):F10-F16 (1999)

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- [X] The following publications were cited in a foreign search or examination report corresponding to PCT/US03/37556:
 - 1. U.S. Publication 2002/0142284, 10/03/2002, Raha et al
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- 3. WO 97/13877
- [X] The following publications were cited in a foreign search or examination report corresponding to EP 02806804.7
 - 1. WO 01/32928, 05/10/2001
 - 2. Database Geneseq [online], "Sindbis virus genomic cDNA PCR primer SEQ ID NO:3," Database Accession No. AAZ92894, retrieved from EBI Accession No. GSN:AAZ92894 (2000)
 - 3. Bulera, S.J., *et al.*, RNA expression in the early characterization of hepatotoxicants in wistar rats by high-density DNA microarrays. Hepatology, 33:1239-1258, (2001)
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- [X] The following publications were cited in a foreign search or examination report corresponding to PCT/US04/025646:
 - 1. Wilson, et al. Exploring drug-induced alterations in gene expression in mycobacterium tuberculosis by microarray hybridization. PNAS 96:12833-12838 (1999)

- 2. Tao, et al., Profiling of differently expressed apoptosis-related genes by cDNA arrays in human cord blood DC34+ cells treated with etoposide. Experimental Hermatology, 31:251-2606 (2003)
- 3. Cadet, et al., Distinct gene expression signatures in the striata of wild-type and heterozygous c-fos knockout mice following methamphetamine administration, Synapset, 44:211-2268 (2002)
- 4. He *et al.*, Histone deacetylase inhibitors induce remission in transgenic models of therapy-resistant acute promyelocytic leukemia., J. Biol. Chem., 276: 20858-20865 (2001)
- [X] The following publications were cited in a foreign search or examination report corresponding to PCT/US04/039593:
 - 1. U.S. Publication 2003/0124552, 07/03/2003, Lindemann et al
 - 2. U.S. 6,132,969, 02/17/2000, Stoughton et al.
 - 3. U.S. 2003/0154032, 08/14/2003, Pittman et al.
 - 4. U.S. 2003/0028327, 02/06/2003, Brunner et al.
 - 5. Hasegawa et al. Gan To Kagaku Ryoho 30: 325-33 (abstract)
- [X] The following publications were cited in a foreign search or examination report corresponding to PCT/US05/034780:
 - 1. Boorman *et al.*, "Toxicogenomics, Drug Discovery, and the Pathologist," Toxicologic Pathology 30(1):15-27 (2002).
 - 2. Harris *et al.*, "Comparison of basal gene expression profiles and effects of hepatocarcinogens on gene expression in cultured primary human hepatocytes and HepG2 cells," Mutation Research 539:79-99 (2004).
 - 3. Gooderham *et al.*, "Molecular and genetic toxicology of 2-amino-1-methyl-6-phenylimidazo[4,5-*b*]pyridine (PhIP)," Mutation Research 506-507:91-99 (2001).
 - 4. Hogstrand *et al.*, "Application of genomics and proteomics for study of the integrated response to zinc exposure in a non-model fish species, the rainbow trout," Comparative Biochemistry and Physiology Part B 133:523-535 (2002).
- [X] The following publications were cited in a foreign search or examination report corresponding to PCT/US05/011532:

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Attorney Docket No. GENE-120/02US Serial No. 10/580,423 Page 8

- 1. Kikuchi *et al.* Gene expression and activities of protein phosphatases 1 alpha, 2A, 2C in hepatocarcinogenesis and regeneration after partial hepatectomy. Cancer detection and prevention. 1997 vol.21(1): 36-43
- 2. Frazier *et al.* Predictive toxicodynamics: empirical/mechanistic approaches. Toxicology in Vitro, 1997, vol. 11: 465-472
- 3. Irizarry *et al.* Summaries of Affymetrix Gene Chip probe level data. Nucleic Acids Research, 2003, vol. 31, page e15
- 4. U.S. 6,153,421
- 5. U.S. 6,421,612
- 6. U.S. 5,858,659
- 7. Jakubczak *et al.* An oncolytic adenovirus selective for retinoblastoma tumor suppressor protein pathway-defective tumors. Cancer Research, 2003 vol 63:1490-1499

This Information Disclosure Statement is filed within any one of the following time periods:

- [] within three months from the filing date of this application;
- [] within three months from the date of entry of the national stage as set forth in 37 C.F.R. §1.491 in this international application;
- [X] before the mailing date of a first office action on the merits; or
- [] before the mailing of a first office action after the filing of a request for continued examination under 37 C.F.R. § 1.114.

It is respectfully requested that the Examiner consider the above-noted information and return an initialed copy of the attached Form PTO/SB/08 to the undersigned.

Respectfully submitted,
COOLEY GODWARD KRONISH LLP

Dated:

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3-2207

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Tel: (202) 842-7800 Fax: (202) 842-7899

By:

Michael S. Tuscan Reg. No. 43,210



PTO/SB/08A (07-05)

Sub	stitute for form 1449A/PTO		Complete if Known
		Application Number	10/580,423
IN	FORMATION DISCLOSURE	Filing Date	May 24, 2006
ST	TATEMENT BY APPLICANT	First Named Inventor	DIGGANS
-		Group Art Unit	1631
	(use as many sheets as necessary)	Examiner Name	To Be Assigned
Sheet	1 of 27	Attorney Docket Number	GENE-120/02US

U.S. PATENT DOCUMENTS						
		U.S. Patent Documen	U.S. Patent Document		Date of Publication of Cited	
Examiner Initials*	Cite No.	Number Kind Code (if known)		Name of Patentee or Applicant of Cited Document	Document MM-DD-YYYY	
•	1.	5,811,231		Farr et al.	09-22-1998	
	2.	5,858,659		Sapolsky et al.	01-12-1999	
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	18.	2003/0154032		Pittman et al.	08-14-2003	
	19.	2003/0028327		Brunner et al.	02-06-2003	

Examiner	Cite	I	oreign Patent D	ocument			T
Initials*	No.	Office	Number	Kind Code (if known)	Name of Patentee or Applicant of Cited Document	Date of Publication of Cited Document MM-DD-YYYY	Т
	20.	wo	93/01205		The Salk Institute for Biological Studies	1-21-1993	1
	21.	wo	94/17208		Xenometrix, Inc.	4-08-1994	Т
	22.	WO	97/13877		Lynx Therapeutics, Inc.	04-17-1997	\Box
	23.	wo	99/27090		Smithkline Beecham Corporation	06-03-1999	
	24.	wo	99/43345		Eisai Co., Ltd.; Beth Israel Deaconess Medical Center	09-02-1999	
	25.	wo	99/58670		Cadus Pharmaceuticals Corporation	11-18-1999	
	26.	WO	00/12760		Incyte Pharmaceuticals	9-3-2000	

^{*}EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. ¹Unique citation designation number (optional). ²See attached Kinds of U.S. Patent Documents. This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

If you need assistance in completing the form, call 1-800-PTO-9199 and select option 2.

Sul	bstitute for form 1449A/PTO	Complete if Known		
		Application Number	10/152,319	
IN	NFORMATION DISCLOSURE	Filing Date	05/22/2002	
S'	TATEMENT BY APPLICANT	First Named Inventor	MENDRICK	
		Group Art Unit	1631	
_	(use as many sheets as necessary)	Examiner Name	C.L. Smith	
Sheet	2 of 27	Attorney Docket Number	GENE-077/22US	

	27.	WO	01/32928	Phase-1 Molecular Toxicology	05-10-2001	
	28.	WO	01/25473	Source Precision Medicine,	04-12-2001	
١				Inc.		1 1

		OTHER – NON PATENT LITERATURE DOCUMENTS
Examiner Initials*	Cite No.	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.
	29.	"nephrotoxic" definition, Merriam-Webster online dictionary, 2005, on the world wide web at http://www.m-w.com/cgi-bin/dictionary?book=Dictionary&va=ncphrotoxic , 2 pages
	30.	Aardema and MacGregor, Mutation Res., 499:13-25, (2002)
	31.	Adamson & Harman et al., Biochem. Pharmacol., 45: 2289-2294 (1993)
	32.	Affymetrix Rat Toxicology U34 Datasheet, released 08/99
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	35.	Ahotupa et al., Carcinogenesis., 15: 863-868 (1994)
	36.	Ala-Kokko, et al., Biochem. J., 244:75-79, (1987)
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_	44.	Anton et al., Cell Biochem. Biophys., 32: 27-36 (2000) Abstract only
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Examiner	48526 v1/DC	Date
is manning.	10520 11150	
Signature		Considered

^{*}EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. ¹Unique citation designation number (optional). ²See attached Kinds of U.S. Patent Documents. This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

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CI	ostitute for form 1449A/PTO		Complete if Known		
Suc	Skitule for form 1449A/FTO	Application Number	10/152,319		
INFORMATION DISCLOSURE STATEMENT BY APPLICANT		Filing Date	05/22/2002		
		First Named Inventor	MENDRICK		
		Group Art Unit	1631		
	(use as many sheets as necessary)	Examiner Name	C.L. Smith		
Sheet	3 of 27	Attorney Docket Number	GENE-077/22US		

		OTHER - NON PATENT LITERATURE DOCUMENTS
Examiner Initials*	Cite No.	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.
	46.	Atchison et al., Digestive Dis. Sci., 45: 614-620 (2000)
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	50.	Barner & Gray, Ann. Pharmacother., 32: 70-77 (1998)
	51.	Bartosiewicz et al., J. Pharmacol. Exp. Ther., 297: 895-905 (2001)
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	56.	Beierschmitt, William P., Induction of Hepatic Microsomal Drug-Metabolizing;, 15-21
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_	58.	Berbner et al., "induction of cytochrome P450 IA and NDA damage in isolated rainbow trout (Onchorhynchus mykiss) hepatocytes by 2, 3, 7, 8-tetrachlorodibenzo p-dioxin," Biomarkers 4: 214-228 (1999)
	59.	Bergeron et al., Xenobiotica, 28: 303-312 (1998)
	60.	Berndt et al., Proc. Natl. Acad. Sci. U.S.A., 95: 12556-12561 (1998)
	61.	Birge et al., Toxicol. Appl. Pharmacol., 105: 472-482 (1990)
	62.	Bissig et al., "Functional expression cloning of the canalicular sulfate transport system of rat hepatocytes," J Biol Chem 269(4):3017-3021, 1994.
	63.	Boelsterli et al., Cell Biol. Toxicol., 3: 231-250 (1987)
	64.	Boess, et al., Toxicological Sciences, 73:386-402, (2003)

Examiner	48526 v1/DC	Date	
Signature		Considered	

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l st	TATEMENT BY APPLICANT	First Named Inventor	MENDRICK
-		Group Art Unit	1631
(use as many sheets as necessary)		Examiner Name	C.L. Smith
Sheet	4 of 27	Attorney Docket Number	GENE-077/22US

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		First Named Inventor	MENDRICK
		Group Art Unit	1631
(use as many sheets as necessary)		Examiner Name	C.L. Smith
Sheet	11 of 27	Attorney Docket Number	GENE-077/22US

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l st	FATEMENT BY APPLICANT	First Named Inventor	MENDRICK
		Group Art Unit	1631
(use as many sheets as necessary)		Examiner Name	C.L. Smith
Sheet	18 of 27	Attorney Docket Number	GENE-077/22US

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Sheet	19 of 27	Attorney Docket Number	GENE-077/22US

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		Application Number	10/152,319	
IN	FORMATION DISCLOSURE	Filing Date	05/22/2002	
STATEMENT BY APPLICANT		First Named Inventor	MENDRICK	
		Group Art Unit	1631	
	(use as many sheets as necessary)	Examiner Name	C.L. Smith	
Sheet	25 of 27	Attorney Docket Number	GENE-077/22US	

		OTHER - NON PATENT LITERATURE DOCUMENTS
Examiner Initials*	Cite No.	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.
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